Neuroscience Trials Newsletter

From the Birmingham Clinical Trials Unit

January 2013

January '13 - Ryan Ottridge

This promises to be an excellent year for our portfolio of PD trials. It is hoped that the recruitment phase for the PD COMM Pilot will finish successfully this Autumn, and during the course of the year we hope to see publications of the PD MED initial results, already presented at our 2011 Collaborators' Meeting, and of the PD SURG and PD MED Health Economics analysis. These should be important publications which will inform the latest NICE guidelines on treating PD.

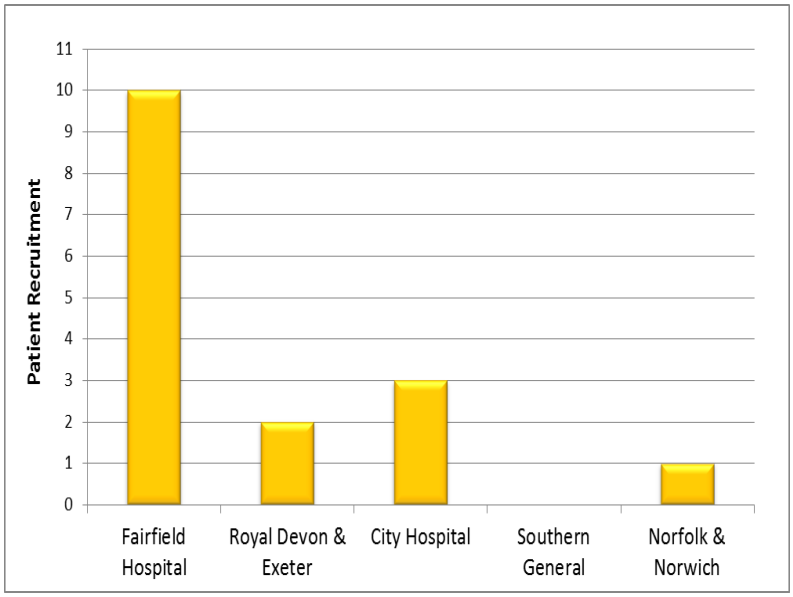
The slowly thawing University of Birmingham campus.

Furthermore, the last PD REHAB patient should complete their follow up this September and if all goes well we may have some initial results from the 3 month data to present by the time of our delayed Collaborators' Meeting after the summer.

Of course, none of this would be possible without the cooperation of all the people who have provided us with data over the last twelve years, so we wish you all a happy New Year and a very big thank you to all of our participants, doctors, nurses, therapists, and other collaborators! Please don't stop returning your questionnaires and annual follow up forms to us!

PD COMM Trial Update - Ryan Ottridge

The PD COMM Pilot, our newest study, has now opened to recruitment at two further hospitals: Southern General Hospital, Glasgow; and Norfolk and Norwich University Hospital. These join Fairfield Hospital, Bury; City Hospital, Birmingham; and Royal Devon and Exeter Hospital who are already open and recruiting, and we wish them all the best in their recruitment to the pilot trial.



So far 16 patients have joined the trial against our final total of 60 — now that we have all of our planned centres open to recruitment, let's hope that we can push on and meet our target by October.

PD COMM Pilot is an investigation into the effectiveness of speech and language therapy in the treatment of Parkinson's — please see our website www.birmingham.ac.uk/pdcomm for more details.

Parky makes more friends, by D. Page

I am not one to put pen to paper but after reading your 3rd trials newsletter where Chris Beards states that he tries to make friends with PD, I couldn't agree more.

Four years ago I had a radical prostate operation and a year later was diagnosed with PD. My new unwanted friend never lets me think about cancer. It's not visual like Parkinson's. The only time of concern is the six months check-up and PSA reading.

Sorry Chris, but I think I have the best carer. We laugh at my antics, especially the old saying "A coffin dodger", I'm a "Door frame dodger" and my stop start walk reminds me of Freddie Star and his "starry starry night" routine.

Getting ready for the day ahead my disability has extended the amount of time spent in the bathroom. Thank god for the electric toothbrush.

Eating causes a few hiccups. Peas don't seem to stay on the fork for too long, so have resorted to a spoon. When the time comes for me to invest in a baby's scoop bib, then my time is up.

Fortunately, I can still drive, although a cloud has settled over the house because of the fact that it's possible my licence will be withheld due to the driving reassessment test and this is after my new photographic licence showing me with a hound dog expression. The family think I look like a hitman for the mafia.

Going up and down ladders has never been a problem for me, nor painting, cleaning or clearing gutters, which is to say that it's been a piece of cake until recently. One length of ladder up against flat roof. Easy job. Two minutes up, clean window, two minutes down. OH NO! Two minutes up, half an hour down, what we call the "parity freeze" had kicked in. Getting on my hands and knees I crawled backwards to the ladder, eventually reaching the ground. Needless to say the ladder has been mothballed.

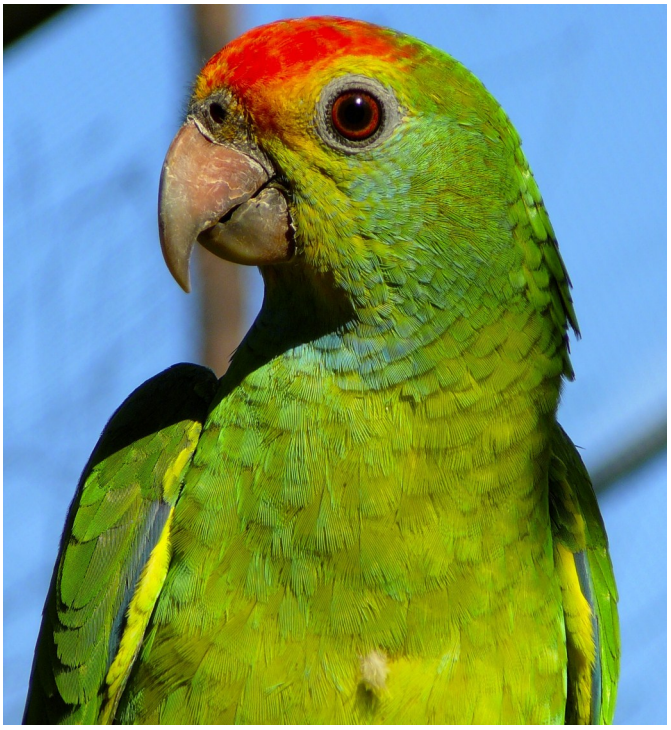
Parkinson's has left my future with an obstacle course. I am fortunate enough to be starting in its early stage, my friendship with "Parky" as we now call it. Both my wonderful wife, who I love dearly, and I will face the challenges ahead.

Would I like Mystic Meg to look in her crystal ball reading the future? NO!

Regards, Derek

P.S. You never know what's around the corner!

That statement has always reminded me of the burglar in the front room of a house who was surprised when a voice said "Jesus is watching you". He shone his torch around and saw a parrot in its cage. "Did you say that?" said the burglar. "I did," said the parrot. "You're a clever parrot," the burglar answered. "I know I am," replied the parrot. "What do they call you?" "Bartholomew," said the parrot. "That's a stupid name for a parrot!" said the burglar. "Well," answered the parrot, "I think Jesus is a stupid name for a Rottweiler!"



Bartholomew the Parrot

Can lifestyle or occupational risk factors affect the risk of developing PD? - Oliver Palin

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease, affecting millions of people worldwide. Despite extensive epidemiological studies to identify causative risk factors, the majority of studies have been largely inconsistent. To date, only age has been identified to be the major risk factor for Parkinson's disease. However, cigarette smoking and coffee consumption have also displayed a consistent association, both apparently reducing the risk. Unfortunately, in the past, too few participants or other methodological limitations have raised questions as to whether these factors can actually reduce the risk.

So can cigarette smoking or coffee consumption really reduce the risk of Parkinson's disease? As you may know, PD GEN has recruited the largest number of Parkinson's disease DNA samples to date. PD GEN participants also fill in an epidemiology questionnaire obtaining information about the patients' and their carers' (if they have one) demographic characteristics, smoking status, caffeine intake, occupational exposures and previous medical history. Therefore, due to this large sample size, we have been able to explore a number of associations with a much greater accuracy than before.

PD GEN collected data on 1359 patients and 682 carer controls. We were able to calculate a risk estimate (in this case an odds ratio) by comparing the history of the patients to the history of the carers. An odds ratio estimates the chance of a particular event occurring in relation to the same event occurring in a different population of people. A statistical programme calculates the risk by providing a number; depending on how far this number deviates from one, it will present us with a large or small risk estimate. So, for example, if an odds ratio is 1.33, it would be interpreted that in one group the outcome is 33% more likely; if an odds ratio is 0.75 then in one group the outcome is 25% less likely (1-0.75=0.25). Adding complexity to this, the risk is only significant if at least 95% of one of the population groups is greater or less than one. For each of the analyses ran, we took into consideration a number of factors which may affect the risk outcome, including Parkinson's disease family history and exposure to pesticides and hydrocarbons.

We found that currently active cigarette smokers significantly reduced the risk of developing Parkinson's disease by 40% when compared to non-smokers, and risk dose-dependently decreased with greater amount of cigarettes smoked per day and total duration of being a current smoker (years). Ex-smokers demonstrated a slightly reduced risk of 13% but were not statistically significant. We then analysed whether coffee or tea remains consistent with the current literature. High coffee drinkers (>1 cup per day) were compared to low coffee drinkers (0-1 cup per day). Drinking 2 or more cups of coffee per day significantly reduced the risk of Parkinson's disease by 24%, which was supported by a significant dose-response relationship. Similarly, high tea consumption was compared to low tea consumption and a reduced odds ratio was observed but did not reach significance.

Also, there are limited data describing the association between occupational exposure to hydrocarbons and the risk of Parkinson's disease. Therefore we compared ever having been occupationally exposed to hydrocarbons for greater than 6 months to having never been exposed. A 47% increased risk was shown, a risk which dose-dependently increased up to 92% when occupationally exposed for greater than 10 years. We conducted a systematic review and meta-analysis of the available data to support this association. A total of 14 case-control studies were identified, including the current study, and pooled a significant summary risk of 1.33 (95% CI 1.12-1.59), suggesting an overall 33% increased risk.

The PD GEN data support the current literature that cigarette smoking and coffee consumption do in fact reduce the risk, and occupational exposure to hydrocarbons increases the risk of developing Parkinson's disease. We stress to our readers to not take up or increase your dosage of smoking as the harmful effects wholly outweigh its beneficial properties. However, the importance of these findings provides evidence for future research to target the mechanism of action of potential neuroprotective agents such as nicotine in cigarettes or caffeine in coffee. This may not only improve the treatment of the symptoms of Parkinson's disease, but may also one day prevent the progression of the disease.

Recruitment and Study Updates - Ryan Ottridge

PD REHAB closed to recruitment in June last year and we are following up patients until September 2013. However, since the main data that we are interested in is the effectiveness of physiotherapy and occupational therapy in the three months after randomisation, the statistics team here in Birmingham have already started on the first batch of analyses.

We don't yet know if we will be able to present these this year—the Data Monitoring and Ethics Committee will decide on this in the Spring. We may have to wait until all follow up is finished in September, but with a bit of luck the first PD REHAB results will be the star of this year's Annual Collaborators' Meeting. This should be held in the Autumn and, of course, details will be sent to all doctors, nurses and therapists as soon as they are finalised. (www.birmingham.ac.uk/pdrehab)

PD GEN had a very successful 2012: we now have 2151 DNA samples from 1438 patients and 713 carers. We should give a very big thank you here to all of our patients and nurses — nearly half of all the patients in our other studies have also taken part in PD GEN. As you can see on page 3 of this newsletter, Oliver Palin, from the University of Birmingham, has done some work on the epidemiological data we have collected from the PD GEN questionnaires. This has been submitted for publication and should come out later in the year. (www.birmingham.ac.uk/pdgen)

PD MED is closed to recruitment but is still collecting information from participants, their carers, and their clinicians. This long term follow up is crucial for the accuracy of future results and establishing best medical practice in people with Parkinson's, so please be sure to continue sending us your questionnaires.

Important notice - The first PD MED results will be published this year. These show that the differences between the drug classes being compared are small and that all of the treatments being compared are reasonable options for people with PD. Results appear at least as good with the older drugs as with the newer, more expensive drugs. But, longer follow-up is needed for definite conclusions. PD is a condition that affects people for many years and, so far, fewer than half of the patients in PD MED have three years or longer follow-up. So, it is important that participants in PD MED stick to their allocated drug class as far as possible so that PD MED will provide definite answers on what drug class provides the best control of disease symptoms, with the least side-effects, over both the first few years and over the longer term. (www.birmingham.ac.uk/pdmed)

Things are also steadily ticking along in PD SURG, our trial looking at the effectiveness of Deep Brain Stimulation in the treatment of Parkinson's. Further work has been done on the previously mentioned STIMULUS algorithm, a potential method of predicting which patients will most benefit from DBS neurosurgery.

Perhaps most excitingly though, we hope to submit the Health Economics analysis soon, and hope to see this in print later in the year. This promises to be a very important publication, answering the question of whether DBS is a cost-effective way of treating the symptoms of Parkinson's. (www.birmingham.ac.uk/pdsurg)

The team still need articles! Please help!

Contact Details

If you're interested in sharing with our community of approximately 2500 doctors, nurses, therapists and participants, please supply your articles, stories or experiences to:

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